REMARKS/ARGUMENTS

Claims 1, 3, 5, and 6 are pending in the application.

Claims 1, 3, 5, and 6 have been rejected under 35 U.S.C. § 103 (a) for alleged obviousness over Gallimore *et al.* Applicants disagree.

To establish a *prima facie* case of obviousness, three requirements must be satisfied: first, there must be some suggestion or motivation to modify the reference or to combine the reference teachings; second, there must be a reasonable expectation of success for achieving the claimed invention and its particular results; and, third, the prior art reference(s) must teach or suggest all the claim limitations. *See In re Vaeck*, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991).

Claims 1, 3, 5, and 6 are directed to methods for the purification of antigen-specific T cells by contacting a MHC class I protein-fluorescent protein ***fusion*** molecule or a ***radiolabeled*** MHC class I protein bound to a specific antigen with a population of T cells, incubating the MHC class I protein bound to the specific antigen together with the population of T cells for a time period sufficient for the T cells to internalize the MHC class I protein from the T cell surface, and identifying T cells that have internalized the MHC class I protein-fluorescent protein fusion molecule or the radiolabeled MHC class I protein.

An example of a MHC class I protein-fluorescent protein fusion molecule recited in the present claims is a MHC class I molecule fused to green fluorescent protein. *See, e.g.*, Specification as originally filed at page 4, lines 12-27. A fusion protein is defined in the art as "[t]he protein product of a gene *created by the fusion of two distinct genes*." LEHNINGER *ET AL.*, in PRINCIPLES OF BIOCHEMISTRY, 2nd Edition, Worth Publishers, New York, 1993, G-6 (emphasis added). An example of a radiolabeled MHC class I protein recited in the present

claims is ^{35}S-labeled MHC class I protein. *See, e.g.*, Specification as originally filed at page 7, lines 16-29; Fig. 2C. It is these ***directly labeled*** MHC class I molecules that form complexes with, or bind to, antigen. Thus, the multimeric complexes internalized by the T cells in the methods recited in the claims include directly labeled MHC class I protein.

In contrast to the present invention, Gallimore *et al.* describes the use of class I-peptide complexes containing mouse class I heavy chain D^b bound to the LCMV peptide epitope glycoprotein (GP)33-41 and biotinylated human ß2 microglobulin ($ß_2M$). As explained in that reference on page 1384 ("Protein Expression and Refolding"), the H-$2D^b$ molecule and the β_2M molecule were independently expressed from separate vectors. Biotinylation of the β_2M molecule was performed by incubation of β_2M molecules with *N*-hydroxysuccinimide biotin. Complex formation was performed by coincubation of the biotinylated β_2M molecules, the H-$2D^b$ molecules, and GP33-41. The complexes were subsequently fluorescent-labeled by coincubation with phycoerythrin-labeled neutravidin, which binds to the biotinylated $ß_2M$ to form a tetrameric complex. *See* Gallimore *et al.*, page 1384, column 1. In other words, Gallimore *et al.* describes a labeled molecule complexed to a MHC class I protein bound in turn to antigen. No MHC class I-fluorescent protein fusion molecule or radiolabeled MHC class I molecule is described or suggested by Gallimore *et al.* Accordingly, Gallimore *et al.* cannot render obvious present claims 1, 3, 5, and 6.

Reliance on the statement in the present specification that "[i]t is also readily apparent to those of ordinary skill in the art that a variety of detectable markers, other than green fluorescent protein, can be fused to the MHC class I molecule, and are suitable for use in the methods of the present invention . . ." (Specification at page 4) to establish the alleged obviousness of the claimed methods is improper. It is a well-established principle of patent

law that the teaching or suggestion to make the claimed modification and the reasonable expectation of success must both be found in the prior art, ***not in applicant's disclosure***. *See In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Accordingly, Applicants assert it is improper to rely on Applicants' disclosure to establish the motivation to modify the teachings of Gallimore *et al.* to arrive at the present invention or the likelihood of success of such a modification. Moreover, the level of skill in the art cannot be relied upon to provide the suggestion to combine or modify references. *See Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 U.S.P.Q.2d 1161 (Fed. Cir. 1999).

Accordingly, Applicants respectfully submit that claims 1, 3, 5, and 6 are patentable over Gallimore *et al.* Applicants request reconsideration and withdrawal of the rejection.

Objections to Figures 1A, 1B, 1C, 1D, 1E, 2A, 2B, 2C, 2D, 3A, 3B, 3C, 3D, 4A, 4B, 4C, and 5 have been made. Applicants submit herewith replacement sheets of those figures. The figures have been amended to comply with 37 C.F.R. § 1.84. No new matter has been introduced by way of this amendment.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a Notice of Allowance at an early date is respectfully requested

If the Examiner believes a telephone conference would expedite prosecution of this application, the undersigned may be contacted at 215-557-5908.

Respectfully submitted,

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Attachments

Replacement sheets for Figures 1A, 1B, 1C, 1D, 1E, 2A, 2B, 2C, 2D, 3A, 3B, 3C, 3D, 4A, 4B, 4C, and 5

LEHNINGER *ET AL.*, in PRINCIPLES OF BIOCHEMISTRY, 2nd Edition, Worth Publishers, New York, 1993, G-6